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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/036,208	10/29/2001	Hiroyuki Odaka	2530 US1P	4444

23115 7590 02/21/2007

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EXAMINER	
ANDERSON, JAMES D	
ART UNIT	PAPER NUMBER
1614	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/21/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/036,208	ODAKA ET AL.	
	Examiner	Art Unit	
	James D. Anderson	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4 and 25-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4 and 25-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/380,059.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' arguments and amendments, filed 10/19/2006, have been entered into the record. Rejections and/or objections not reiterated from previous Office Actions are hereby withdrawn. However, upon further consideration, the following rejections and/or objections are newly applied. They constitute the complete set presently being applied to the instant application.

Status of the Claims

Claims 4 and 25-27 are currently pending and are the subject of this Office Action.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 4 and 25-27 are rejected under 35 U.S.C. § 102(a) as being anticipated by WO 98/11884 (prior art of record).

The reference discloses that insulin-sensitizing agents (*e.g.* pioglitazone) can be used in combination with sibutramine to treat diabetes, impaired glucose intolerance and complications of diabetes in which insulin resistance is present (pages 12-13).

The instantly claimed method of reducing glycosylated hemoglobin levels is inherently taught by the reference. When sibutramine and pioglitazone are administered in combination to

a patient with diabetes as taught in the reference, a reduction in glycosylated hemoglobin levels is a natural result of such administration.

It is noted that *In re Best* (195 USPQ 430) and *In re Fitzgerald* (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter, which there is reason to believe inherently includes functions that are newly cited, or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter to be shown in the prior art does not possess the characteristic relied on" (205 USPQ 594, second column, first full paragraph). There is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference. *Schering Corp. v. Geneva Pharm. Inc.*, 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003); see also *Toro Co. v. Deere & Co.*, 355 F.3d 1313, 1320, 69 USPQ2d 1584, 1590 (Fed. Cir. 2004) ("[T]he fact that a characteristic is a necessary feature or result of a prior-art embodiment (that is itself sufficiently described and enabled) is enough for inherent anticipation, even if that fact was unknown at the time of the prior invention").

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The instant claims are drawn to a method of lowering glycosylated hemoglobin levels in mammals through the administration of pioglitazone and sibutramine. The evidence of unexpected results (demonstrated in the 37 C.F.R. 1.132 Declaration of Dr. Okada) has been reconsidered and is not deemed to be sufficient to overcome the prior art. The data shown in Table 1 of the Declaration is unclear with respect to the results that have been shown. For example, the "-" sign in front of the numerical values indicates that a negative amount of plasma glucose and plasma triglycerides was found. Clearly, one cannot have negative plasma glucose and plasma triglycerides. In addition, with respect to "HbA1 c(%)", it is not clear what the data are showing. Are the values intended to show percent glycosylated hemoglobin or the *decrease* in glycosylated hemoglobin? Similarly, with respect to plasma glucose and triglycerides, it is not apparent whether the values in the table are changes or numerical values (*i.e.* amount = mg/dl). The Declaration, taken as a whole, raises questions with respect to whether unexpected results have been demonstrated. Applicants are requested to clarify the data presented in the Declaration of Dr. Okada, specifically the results shown in Table 1.

Claims 4 and 25-27 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Grossman *et al.* (Exp. Opin. Invest. Drugs, 1997, vol. 6, pp. 1025-1040) (prior art of record) and Hauner (International Journal of Obesity, 1999, vol. 23, Suppl. 7, pages S12-S17) in view of WO 93/03724 (prior art of record).

Grossman *et al.* review the mechanisms and clinical effects of thiazolidinediones in the treatment of diabetes mellitus. The insulin-sensitizer pioglitazone is disclosed as decreasing hyperglycaemia, hyperlipidaemia, hyperinsulinaemia and glucose intolerance in genetically obese and diabetic yellow KK mice and Zucker fatty rats (p. 1027, left column, first paragraph of Section 3.2). The clinical effects of the thiazolidinedione troglitazone demonstrated a significant decrease in HbA_{1c} supporting the concept that "thiazolidinediones can improve hyperglycaemia through decreased insulin resistance, as well as favourably influencing lipid metabolism" (p. 1032, second paragraph under Section 5.1.2). It is noted that the instant specification defines glycosylated hemoglobin as "HbA_{1c}" on page 32, line 33. The thiazolidinedione pioglitazone has been shown to reduce mean HbA_{1c} over 12 weeks in two Japanese dose-ranging studies (p. 1034, Table 4 and Figure 1). The reference does not disclose administration of pioglitazone and the anorexiant, sibutramine, in combination to reduce glycosylated hemoglobin.

However, Hauner discloses that the anorexiant sibutramine produced dose-related weight reduction and improved HbA_{1c} levels in randomized clinical trials (page S15).

The motivation to combine the references is found in WO 93/03724 wherein the authors state that, for the treatment of diabetes and disorders related to diabetes, what is needed is "a therapy that may be used in combination with anti-diabetic drugs to treat or prevent obesity, resulting from treatment with an insulin sensitizing drug or an insulin secretion stimulating drug" (p. 5, lines 9-11).

It is generally obvious to combine two compositions, each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose. *In re Kerkhoven*, 205 U.S.P.Q. 1069 (CCPA 1980). The idea for combining said

compositions flows logically from their having been individually taught in the prior art. *In re Crockett*, 126 U.S.P.Q. 186, 188 (CCPA 1960).

Accordingly, to establish obviousness in such fact situations it is NOT necessary that the motivation come explicitly from the reference itself (although the Examiner believes it does, as discussed supra). The natural presumption that two individually known antidiabetic agents would, when combined, provide a third composition also useful for treating diabetic conditions, including reducing HbA_{1c} levels, flows logically from each having been individually taught in the prior art. Applicant has presented no evidence (*e.g.* unexpected results) to rebut this natural presumption.

Thus, the present invention of lowering the level of glycosylated hemoglobin (HbA_{1c}) by administering a combination of pioglitazone and sibutramine would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made. Examiner notes that the instant method can be achieved with the instantly claimed insulin-sensitizing agent alone - the addition of an anorectic is not essential for the lowering of glycosylated hemoglobin.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James D. Anderson whose telephone number is 571-272-9038. The examiner can normally be reached on MON-FRI 9:00 am - 5:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

James D. Anderson, Ph.D.
Patent Examiner
AU 1614

February 14, 2007

Phyllis Spivack

PHYLLIS SPIVACK
PRIMARY EXAMINER